BY ORDER OF THE SECRETARY OF THE AIR FORCE

AIR FORCE INSTRUCTION 40-403

19 MAY 1994

Medical Command

CLINICAL INVESTIGATIONS IN MEDICAL RESEARCH GUIDANCE AND PROCEDURES

COMPLIANCE WITH THIS PUBLICATION IS MANDATORY

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Certified by: AFMOA/SGP
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This instruction implements AFPD 40-4, *Clinical Investigation and Human Use in Medical Research*. It provides guidance and procedures for conducting clinical investigations at medical treatment facilities (MTF), clinical investigation facilities (CIF), and other medical support centers. It establishes procedures for using human subjects as volunteers in scientific studies in the Medical Service. If you will be using animals in clinical investigations, refer to AFI 40-401, *The Use of Animals in DoD Programs*. Refer to AFI 40-402, *The Use of Human Subjects in Research, Development, Test, and Evaluation (RDT&E)* when using human subjects in RDT&E studies. **Attachment 1** lists references, abbreviations, acronyms, and terms used in this instruction.

SUMMARY OF REVISIONS

This is the initial publication of AFI 40-403, aligning it with AFPD 40-4.

Chapter 1

RESPONSIBILITIES

1.1. The Air Force Surgeon General (HQ USAF/SG):

- Appoints a Clinical Investigation Committee (CIC) to review and approve or disapprove all clinical investigation proposals.
- Monitors the Air Force Clinical Investigation Program (CIP).
- Authorizes annual funds to support the Air Force CIP.

1.2. The Surgeon General's Clinical Investigation Committee:

- Reviews and approves or disapproves all proposals not involving investigational use of drugs, devices, and radiopharmaceuticals.
- Reviews clinical investigation proposals involving investigational drugs, devices, and radiopharmaceuticals and makes recommendations to the Air Force Surgeon General for final approval.
- Authorizes funds for each protocol's resource requirements.
- Coordinates on emergency-use protocols.
- Submits approvals, disapprovals, and recommendations to the MTF for implementation or action.
- Reviews offers of gifts and grant applications for clinical investigations, and processes them through the Office of the Secretary of the Air Force for final approval.

1.3. Major Command (MAJCOM):

1.3.1. Air Mobility Command (AMC) establishes and operates a CIF in conjunction with the David Grant Medical Center and a CIP at the Malcolm Grow Medical Center and Medical Center Scott.

1.3.2. Air Force Materiel Command (AFMC) establishes and operates a CIP in conjunction with the Medical Center Wright-Patterson.

1.3.3. Air Education and Training Command (AETC) establishes and operates CIFs in conjunction with the Keesler Medical Center and Wilford Hall Medical Center.

1.4. Medical Facility Commander (MTF/CC):

1.4.1. Ensures compliance with Code of Federal Regulations (CFR), Title 32, Part 219, *Protection of Human Subjects*.

1.4.2. Establishes an Institutional Review Board (IRB).

1.4.3. Approves or disapproves clinical investigation proposals after they are reviewed by the IRB. If an IRB stipulates safeguards or special conditions to a protocol that it recommends for approval, the approving authority may not reduce these safeguards or conditions when it approves the protocol. The approving authority may require additional safeguards, disapprove the protocol, or, may refer it to a higher review committee and approval authority.

1.4.4. Appoints a medical or dental officer other than the investigator to be responsible for advising the subject of his or her rights if necessary. The advising medical or dental officer must be neither directly associated with the investigation nor be under the control of the investigator.

1.4.5. Sends the following numbers of copies of IRB-approved clinical investigation proposal, including appropriate attachments, to Headquarters Air Force Medical Operations Agency, Clinical Investigations and Life Science Division (HQ AFMOA/SGPT), 170 Luke Avenue Suite 400, Bolling AFB DC 20332-5113:

- Four copies of human-use protocols and five copies of animal-use protocols, with one copy of the principal investigator's curriculum vitae.
- For National Cancer Institute-sponsored protocols (such as Southwest Oncology Group), one copy.
- One information copy to the command surgeon.

1.4.6. Ensures that the Office of the Surgeon General approves an investigation before research is begun. Makes sure all changes directed by the Surgeon General's CIC are accomplished.

1.4.7. Makes sure that the equipment provided to the MTF by the Surgeon General's CIC is properly obtained and used.

1.4.8. Helps approved clinical investigations proceed as planned.

1.4.9. Makes sure the Surgeon General's CIC approves any deviations from the approved protocol.

1.4.10. Approves new investigators on approved protocols, based on the MTF IRB recommendation, and provides relevant information, including the new investigator's curriculum vitae, to HQ AFMOA/ SGPT.

1.4.11. Ensures that a copy of all progress and final reports (**Attachment 6**) are sent to HQ AFMOA/ SGPT, and to the command surgeon.

1.5. Institutional Review Board:

1.5.1. Reviews all clinical investigation protocols to determine their scientific merit and whether the use of subjects is acceptable.

1.5.2. Ensures that applications and approvals for the use of investigational drugs and devices comply with Food and Drug Administration (FDA) regulations.

1.5.3. Sends its approval or disapproval of the protocol to the medical facility commander or appointed representative.

1.5.4. Reviews the conduct of the study at least once a year.

1.5.5. Maintains records of:

- Clinical investigation proposals reviewed or approved.
- Informed consent documents for all subjects.
- Progress and final reports submitted by investigators.
- Reports of injuries to subjects.
- Minutes of IRB meetings. These must be detailed enough to show who attended the meetings; what actions the IRB took; the vote count on actions, including the number of members voting

for, against, and abstaining; the basis for disapproval or required changes in research; and a summary of the discussion of issues and their resolutions.

- Records of continuing review activities.
- Copies of all protocol-related correspondence.
- A list of IRB members identified by name, office, earned degrees, and in what capacity they are present.

1.5.6. Appoints, at least annually, committee personnel to spot-check the medical records of study subjects. This group verifies that the investigators have filed signed informed consent documents in the medical record and have recorded pertinent health care information. Reports of these spot checks are provided in writing to the chairperson of the IRB.

1.5.7. Reviews all progress and final reports submitted to the IRB by the principal investigator.

1.5.8. If the principal investigator is reassigned, separates, or retires, the IRB:

- Arranges for a new principal investigator to continue the project, if practicable.
- Ensures that the principal investigator submits a final report concerning the status of the clinical investigation.

1.6. The Department Chairperson:

1.6.1. Helps departmental staff resolve ethical conflicts that may arise between biomedical or behavioral research, and the accepted and routine practice of medicine.

1.6.2. Approves protocols proposed by the department staff.

1.7. The Principal Investigator:

1.7.1. Prepares the Protocol Summary (**Attachment 2**), Proposal for Clinical Investigation (**Attachment 3**) and, if required, Informed Consent Document (**Attachment 4**) and submits them to the MTF commander through the medical facility IRB. If the IRB and the medical facility commander approve the study, the summary, informed consent document, and proposal are then submitted to HQ AFMOA/SGPT for review by the Surgeon General's CIC.

- If the investigation is to evaluate a new drug or device according to 21 CFR, parts 300-499, the investigator must submit the appropriate forms to the FDA. The protocol cannot begin until both the HQ USAF/SG and the FDA have given their approval to the submitting facility.
- If the investigator already has received an Investigational New Drug number (IND) or Investigational Device Exemption (IDE) number from the FDA, or if the manufacturer holds the IND or IDE, the IND/IDE number must be cited in the protocol.

1.7.2. Complies with all policies concerning the use of human subjects during the course of the investigation.

1.7.3. Performs and supervises the conduct of the investigation and records data relating to the investigation, as required. These records include a notebook listing:

- All studies performed
- Dates performed
- Quantity of drugs administered

- Names of participants
- Test results

The principal investigator must give a copy of significant notebook entries to the IRB to include in the clinical investigation protocol records when the project ends.

1.7.4. Maintains records and submits reports required by the FDA, when conducting studies as part of an IND

1.7.5. Documents the medical and dental care given to the patient under the study. You must maintain the patient's medical or dental record as you would in standard medical/dental practice. A copy of the volunteer's informed consent must be on file in the medical or dental record. Special entries may be added to alert any other health care providers who may treat the patient to particular characteristics or reactions that may result from the investigational treatment.

1.7.6. Submits all proposed changes to the protocol or to the informed consent document to the IRB. The IRB must approve changes before they are implemented.

1.7.7. Submits one copy of the following reports to HQ AFMOA/SGPT through the local IRB and to the command surgeon or designated approving authority:

- Annual progress reports, including a copy of any study-related abstract, oral presentation, technical report, or journal article. You must submit a separate report on each clinical investigation study.
- A final report of the findings and conclusions when investigation is completed or if it is terminated before completion. Make suggestions for application and possible additional research, where appropriate.

Chapter 2

THE SCOPE OF THIS INSTRUCTION

2.1. Investigations Covered by This Instruction:

2.1.1. Clinical investigations involving the biological, behavioral, or psychological study of a person's body or surroundings, conducted by or together with Air Force Medical Service personnel. These include, but are not limited to:

- Medical or surgical procedures.
- Withdrawal or removal of body tissue or fluid.
- Administration of all chemical or biological substances.
- Deviation from normal diets or daily regimens.
- Active manipulation of bodily processes, behavior, or environment.

2.1.1.1. Examples of clinical investigations are:

- Studies representing a deviation from accepted practice but specifically aimed at improving diagnosis, prevention, or treatment of a patient's specific illness.
- Studies related to a patient's disease but from which the patient may not receive any direct benefit.
- Investigative, non-therapeutic studies in which there is no intent or expectation of treating a patient's illness.
- Investigative, non-therapeutic studies in which the subject is a "normal control" who is not suffering from an illness but has volunteered to participate for the potential benefit of others.
- Field trials of vaccines and prophylactic drugs.

2.1.2. Use of drugs, devices or radiopharmaceuticals that are not approved by the FDA, or use of FD-Aapproved drugs, devices, or radiopharmaceuticals in a manner not provided for in the FD-Aapproved indications. Using FD-Aapproved drugs, devices or radiopharmaceuticals for therapeutic effects that are widely reported and are generally accepted within the scope of normal medical practice, does not constitute clinical investigation or research in the sense of this instruction.

2.1.3. Emergency use of investigational drugs or devices.

2.2. Investigations Not Covered by This Instruction:

2.2.1. Use of human subjects in the Air Force RDT&E Program where:

- The diagnostic and treatment procedures use techniques or therapeutic regimens that conform to accepted professional practice.
- All medications or devices will be used within the FD-Aapproved indications for the drug or device involved, or come within the exception inparagraph **2.1.3.**

2.2.2. This instruction also does not apply to studies involving the following types of data collection, unless specific individuals are identified in the data as published or presented:

- Statistical information from patients' records.

- Passive observation of biological, physiological, or behavioral parameters.
- Subjects' responses to questionnaires or surveys. You must obtain appropriate clearance procedures before you publish or present the data (see AFI 36-2601, *Air Force Personnel Survey Program*).
- Educational testing (cognitive, diagnostic, aptitude achievement).
- Analysis of excreta.
- Epidemiological studies (AFI 48-112, *The US Air Force Hyperbaric Medicine Program*) that involve no more than minimal risk, as set forth in human protection regulations issued by the Department of Health and Human Services (CFR, Title 45, Part 46).
- Analysis of any specimen of tissue or body fluid that was collected during normal medical or surgical management of a patient and did not subject the patient to additional or duplicate tests, procedures, or treatments.
- Necropsy material.

2.2.3. Purely diagnostic use of radiopharmaceuticals that are FD-Aapproved, used in a widely reported and generally accepted manner, and within the scope of normal medical practice, do not constitute clinical investigations in the sense of this instruction. However, innovative uses of radiopharmaceuticals for clinical investigative studies, must be approved by a radioisotope committee, and must comply with Nuclear Regulatory Commission requirements.

Chapter 3

USE OF HUMAN SUBJECTS IN CLINICAL INVESTIGATIONS

3.1. Guidelines for the Use of Human Subjects. The requirements listed here apply to the use of human subjects in MTFs and CIFs.

3.1.1. The investigator must:

- Safeguard the rights and welfare of the subject throughout the investigation.
- Ensure that risks to the subject are minimized and considered reasonable when compared to potential benefits of the study, including any potential medical advances.

3.1.2. The investigation must be impossible without the participation by a human test subject. The investigator must conduct and evaluate all necessary preliminary tests with laboratory animals and human simulators, insofar as possible, before using a human test subject.

3.1.3. The investigator must avoid all unnecessary physical or mental discomfort to human subjects, by planning for adequate facilities and making proper research preparations. Studies are not permitted if there is significant possibility that the subject could suffer disease, injury, or death. The investigator must:

- Conduct an evaluation of the subject before the study begins and record the results.
- Use the minimum number of subjects required for statistical significance in conducting the study.

3.1.4. When circumstances warrant, the medical facility commander may appoint a medical or dental officer other than the investigator to ensure that you conduct the study properly and take professional care of the subject.

3.1.5. The principal investigator, normally a physician, dentist, biomedical scientist, or nurse, must ensure that the subject has the capacity to consent, is able to exercise true freedom of choice without overt or hidden persuasion, and is fully informed.

3.1.6. Before a subject is permitted to give consent, the investigator or associate investigator must accurately explain the investigation in language the subject can understand. This explanation must be made a part of the informed consent document.

3.1.6.1. The informed consent document should contain, in addition to the components identified in 32 CFR 219, the following statements:

- Any medical misadventure or unanticipated medical event will be brought immediately to the attention of the subject, or the subject's guardian or next of kin, if the subject is not competent at the time to understand the nature of the misadventure or unanticipated medical event.
- Records of the study may be inspected by the FDA or sponsoring institution, if appropriate.

3.1.7. Informed Consent. The subject must give consent in writing. The investigator must attach a copy of the voluntary consent form to the protocol using these procedures:

3.1.7.1. The subject must sign the consent form in the presence of at least one witness, who attests to the subject's signature by signing in the place provided. If the subject is military (whether active duty or retired), enter the social security number (SSN)of the subject on the form under the subject's signature. If the subject is a military dependent, enter the SSNs of both the military sponsor and the dependent, if available, on the form under the subject's signature.

3.1.7.2. The investigator or associate investigator gives the advice that forms the basis for the informed consent. This individual must sign the consent form in the presence of the same witness.

3.1.7.3. Sign or reproduce the consent document in at least four copies. Give a copy to:

- The IRB.
- The subject's medical record.
- The investigator.
- The subject.

3.1.7.4. The investigator must obtain medicolegal consultation on each consent document during the protocol review process.

3.2. Approval of Clinical Investigations. With the exceptions noted in paragraph **2.2.2.**, **4.1.**, and **7.1.**, HQ AFMOA/SGP must review and approve all clinical investigations prior to their inception.

3.3. Federal Statutory Limitations. Federal law limits the use of subjects in Department of Defense (DoD) or Do-Dsupported research to persons who are fully informed and who voluntarily agree to participate in the study. If the patient is legally incompetent to give consent (as with infirm elderly, minors, or patients in an unconscious state) and the proposed measures are intended to directly benefit the subject, then consent may be obtained from a legal representative on the subject's behalf.

3.4. Active Duty Personnel as Human Subjects. The investigator, in consultation with the subject, should determine whether participation in a study would affect the ability of the subject to mobilize for readiness, to perform duties, or to be available for duty. Normally, if their participation could affect their performance, they should not be considered for the clinical investigation.

3.4.1. Active duty personnel may not be compensated for participation, except according to 24 U.S.C. 30.

3.5. Minors as Human Subjects. Minors may be used as subjects only when the clinical investigation is intended to be of direct benefit to the subject and satisfies one of the categories in **3.5.1.** or **3.5.2.** of this instruction. In both cases, the investigator must solicit the assent of the minor according to **3.5.3.**, as well as the consent of one or both parents or guardian according to **3.5.4.**

3.5.1. The investigation must present no greater than minimal risk to the minor subject.

3.5.2. The investigation may present greater than minimal risk to minor subjects if the proposed procedures hold out a prospect of direct benefit to the individual subject, and if the IRB finds that:

- The risk is justified by the anticipated benefit to the subject.
- The relationship of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches.

3.5.3. In some cases, minor subjects may be mature enough to understand the nature and consequences of their participation, or nonparticipation, in the study. The IRB must ensure that in these cases the investigators solicit the minor's consent, as well as the parent or guardian's, before performing a medical procedure. The investigator should assess the age, maturity, psychological state, and mental capacity of the minor subjects potentially involved in a study to determine if their consent has legal merit. Consult the legal advisor where a minor subject's capability to assent is in question.

3.5.4. For studies involving minor subjects, the IRB generally should provide for the documented informed consent of both parents or the guardian of the minor subject.

3.6. Mentally Disabled Persons as Human Subjects:

3.6.1. A mentally disabled or institutionalized mentally infirm person may not participate as a test subject, unless the study would be impossible or meaningless if such subjects were excluded. The investigator may not use any such person as a test subject purely for the sake of convenience.

3.6.2. A mentally disabled or institutionalized mentally infirm person may not participate as a test subject unless:

3.6.2.1. The subject has given legally effective consent, or the subject's legally authorized representative has given effective third part consent, according to local law.

3.6.2.2. The proposed study is concerned with one or more of the following:

- The diagnosis, treatment, prevention, or etiology of a particular impairment that inflicts the subject.
- Any other condition from which the subject is suffering, provided there is a direct potential benefit to the subject, and prior testing has proved the risk to be acceptable.
- The effect of institutional life on the institutionalized mentally infirm subject, and involves no appreciable risk to the subject.
- Information which cannot be obtained from any other class of subjects.

3.6.3. If the mentally disabled or institutionalized mentally infirm person appears to have sufficient mental capability to comprehend what is proposed and is able to express his or her willingness to participate, the investigator should obtain consent.

3.7. Prisoners as Human Subjects. A prisoner may not participate as a human subject unless the proposed clinical investigation is concerned with the diagnosis, treatment, prevention, or etiology of a particular impairment that afflicts the prisoner and unless the prisoner may derive a direct potential benefit.

3.8. Prisoners of War as Human Subjects. The use of prisoners of war is prohibited unless approved by the Office of the Under Secretary of Defense for Acquisition (OUSDA).

3.9. Non-US Citizens as Human Subjects. In clinical investigations conducted outside the United States involving non-US citizens as human subjects, the laws, customs, and practices of the country in which the study is conducted, or those required by this instruction, whichever are more stringent, shall take precedence. The study shall meet the same standards of ethics and safety that apply to studies conducted within the United States, involving US citizens.

3.10. Protocols Involving Nuclear Weapons Effects or Chemical Warfare Agents. Such protocols involving human subjects must be submitted to OUSDA for approval prior to implementation.

Chapter 4

EMERGENCY USE OF AN INVESTIGATIONAL DRUG OR DEVICE

4.1. Procedures:

4.1.1. Comply with all FDA procedural requirements when using the investigational drug or device. The using physician is the agent responsible for following these FD-Aprescribed actions outlined below.

4.1.2. Submit a formal request for approval (**Attachment 4**) to the MTF commander, describing the lifethreatening situation and why the absence of standard acceptable treatment is not adequate or appropriate. When possible, obtain the approval prior to using the drug or device.

4.1.3. Submit this approval and the request for emergency use to the IRB within 5 workdays. The IRB reviews whether the emergency use is appropriate, makes recommendations as needed to MTF personnel, and sends the request for emergency use, with the MTF commander's approval and the IRB recommendations, to HQ AFMOA/SGPT.

4.1.4. Submit a formal protocol when multiple patients will receive the same investigational drug or device.

Chapter 5

BUDGETING AND FUNDING

5.1. Funding Source. Use operations and maintenance funds for operating the clinical investigation facilities.

5.2. Budgeting Responsibilities:

- The MAJCOM budgets and funds the clinical investigation program at each of their medical centers.
- Funds provide a laboratory work environment suitable for conducting clinical investigation studies.
- Funds purchase basic equipment and supplies that are essential for a clinical investigation facility.

5.3. The Surgeon General's Clinical Investigation Committee:

5.3.1. Provides funds to support approved investigational protocols that have unique supply, equipment, or service requirements.

5.3.2. Funds for clinical investigations normally are not used to hire additional personnel, to cover the cost of reprints, or for temporary duty travel.

5.3.3. Submit requests for investment equipment requirements, not expressly identified as a part of a specific clinical investigation proposal, to the MAJCOM as part of the annual investment equipment budget of the base medical services.

5.3.4. The Surgeon General's CIC has final disposition authority for all committee-approved unexpended funds and committee-funded investment equipment.

5.4. The Air Force Medical Logistics Office (AFMLO). Processes and manages the investment equipment items specifically included in proposals approved by the Surgeon General's CIC.

5.4.1. Coordinate these requests with the local medical equipment management office (MEMO). MEMO will forward the AF Form 601, **Equipment Action Request**, through MAJCOM channels to the AFMLO.

5.4.2. Attach a copy of AF Form 601, and appropriate equipment documents to the protocol. This serves as justification for the requirement and will reduce the time needed for the coordination.

5.4.3. List requests for funding of contracted services, (laboratory tests not accomplished at the local MTF, for example) under supplies and equipment.

Chapter 6

COLLABORATIVE INVESTIGATIONS WITH NON-AIR FORCE ORGANIZATIONS

6.1. Agencies Effected. Collaborative studies with non-Air Force federal agencies or civilian organizations that involve patients at Air Force MTFs or that are conducted at Air Force MTFs must comply with this instruction. For example, such studies must have an Air Force principal investigator (or co-principal investigator) and must be reviewed by the local IRB and approved by the Surgeon General's CIC.

6.2. Air Force Personnel:

6.2.1. May act as investigators in studies conducted outside of Air Force MTFs only if the medical facility commander decides it is in the best interest of the Air Force. If such studies involve human subjects, the sponsoring facility's IRB must review and approve the study according to Federal law and regulations.

6.2.2. Send a copy of the sponsoring facility's request for Air Force medical service personnel participation and the commander's approval to HQ AFMOA/SGPT.

Chapter 7

BLANKET APPROVAL FOR NATIONAL ONCOLOGY STUDY GROUPS

7.1. Approving Authority:

7.1.1. The Air Force Surgeon General may: Provide blanket approval for specific national oncology groups.

7.1.1.1. If approved by the IRB and MTF/CC, the investigator may enroll patients into the study before submitting the protocol to the Surgeon General's CIC.

7.1.1.2. Assurance must be valid before approving oncology study group protocols.

7.1.1.3. The MTF IRB ensures that the MTF has a valid assurance number in effect from the NIH and Office for Protection from Research Risks.

7.2. Termination of Oncology Protocols. Oncology protocols terminate after the protocol is closed to new patient registration, and all patients entered into the study have completed treatment.

Chapter 8

REPORTING OF MEDICAL MISADVENTURES OR UNANTICIPATED MEDICAL EVENTS

8.1. MTF Commander Responsibilities:

8.1.1. Reports any misadventures or unanticipated events involving a clinical investigation study within 5 workdays.

8.1.2. Submits a *Medical Misadventure Report* (RCS: HAF-SGE[AR]8501) to:

- HQ AFMOA/SGPT.
- The appropriate command surgeon.
- The area medical law consultant.

8.1.3. Electronically sends initial reports as quickly as feasible to the above addressees if the misadventure or unanticipated event is lifethreatening or otherwise serious.

8.1.4. Uses the most expeditious alternative available to make reports if MINIMIZE is imposed.

8.1.5. Submits a complete narrative report to the above addressees within 15 workdays of the misadventure. If the reports are not classified, mark them FOR OFFICIAL USE ONLY and SENSITIVE MEDICAL DATA.

Chapter 9

NATIONAL INSTITUTES OF HEALTH (NIH) GRANTS

9.1. Application Procedures:

9.1.1. Investigators may apply for NIH grants.

9.1.2. Requires Office of the Secretary of the Air Force approval before submittal.

9.1.3. Send application, along with the locally approved investigative protocol, including attachments, to the Surgeon General's CIC for approval.

9.1.4. HQ AFMOA/SGPT sends the protocol and application to the Secretary of the Air Force for approval.

9.2. Types of NIH Funding:

9.2.1. Direct Funding. If funds are awarded, establish specific accounting criteria for audit trails at the local institution.

9.2.2. Indirect Funding. MTFs that have institutional membership with civilian agencies, such as national cancer groups or medical and dental schools, may receive the benefits of NIH funds awarded to the parent institution. In those cases where the parent institution receives and controls funds, the Air Force facility participating in the study may receive support. This indirect funding mechanism does not require Office of the Secretary of the Air Force approval, as prescribed above, since NIH funding to the parent institution is not directly under Air Force management.

Chapter 10

CLINICAL INVESTIGATION STUDIES INVOLVING GIFTS, INCLUDING GRANTS FROM SOURCES OTHER THAN NATIONAL INSTITUTES OF HEALTH

10.1. Gift Policy:

10.1.1. The MTF/CC may accept gifts of a value of $5,000 or less that require only a small expenditure to accept and maintain (see AFI 51-601, *Gifts to the Air Force*).

10.1.2. Only the Secretary of the Air Force may accept a gift offer with a value over $5,000 (AFI 51-601). Send the signed letter from the donor offering the gift and the protocol through the MTF IRB and the MTF commander to HQ AFMOA/SGPT.

10.1.3. Federal law allows gifts to be accepted use with MTF operations. To avoid the appearance of impropriety or violation of law, all gifts and benefits, including funds for travel, offered in connection with clinical investigations must be fully disclosed and accepted according to AFI 51-601.

10.1.4. Do not make arrangements to grant special privileges or concessions to the donor. Clinical investigations conducted by Air Force personnel or in Air Force MTFs must meet the criteria in **2.1.** and any benefit derived by the general public or non-DoD organizations must be coincidental to Air Force objectives. If you accept a gift in connection with the conduct of a particular Air Force clinical investigation, you must advise the donor that the investigation may be delayed or terminated if necessary in the interest of meeting Air Force mission requirements.

10.1.5. The Air Force policy that prohibits you from soliciting gifts does not prohibit you from applying for standard grants. However, the terms of any such grant applications must be consistent with the policies of this paragraph and AFI 51-601.

10.1.6. Gifts may be rejected under circumstances described in AFI 51-601.

10.1.7. If the donor is a defense contractor or subcontractor, the donor must state that the cost of the gift will not be charged either directly or indirectly, as an element of cost in any US Government contract.

10.1.8. The officer in charge of the MTF CIP, or other officer designated by the MTF commander will administer gifts received in connection with Air Force clinical investigations. Prospective donors should contact this officer for guidance on proper procedures for making gifts offers. To avoid an actual or apparent conflict of interest, principal or associate investigators or others directly involved in a clinical investigation must not directly accept or administer gift funds accepted from the donor for use in connection with the clinical investigation.

10.2. Gift Procedures:

10.2.1. A legal representative of the donor must sign gift offers with a value over $5,000. The level of certification will be appropriate to the value of the gift. All gift offers will accompany the clinical investigation protocol through the MTF IRB and the MTF commander, to the Surgeon General's CIC.

10.2.2. The MTF/CC recommends that the gift be accepted or rejected.

10.2.3. The Surgeon General's CIC reviews the offer and any relevant information, requesting additional information as needed. The CIC recommends that the gift be accepted or rejected and forwards

the offer to the Office of the Secretary of the Air Force for final approval, as required under AFI 51-601.

10.2.4. If the gift is accepted, the MTF/CC must ensure that proper actions are taken to receive and establish accounting for the gift.

10.2.5. If the gift is tangible property, such as equipment, follow receipt and accounting procedures.

10.2.6. If the gift is money, receive and deposit the funds to the Trust Fund Receipt Account, 578928, Deposits, Department of the Air Force Gift Fund. Send a copy of DD Form 1131, **Cash Collection Voucher**, or Standard Form 1081, **Voucher and Schedule of Withdrawals and Credits**, to the Defense Finance and Accounting Service (DEFAS), 6760 East Irvington, Denver CO 80279-7000, with a request to issue Allocation Authority documents. Do not spend funds until DEFAS issues a Budget Authorization or Allocation.

10.2.7. Donors may give a wide variety of administrative, technical, or professional services to the Air Force as "Gifts of Service," in support of a clinical investigation protocol or program, and at no cost to the government.

10.2.7.1. The Office of the General Counsel has determined that the gift statute (10 U.S.C. 2601) and AFI 51-601 do not cover services, as provided by civilian employees or agents of nonfederal organizations, such as national cancer study groups

10.2.7.2. To avoid any appearance of impropriety or violation of law, prepare gifts of technical assistance offered in support of a clinical investigation according to **Attachment 7** of this instruction. The Judge Advocate General office servicing the MTF prepares the appropriate legal document to accept proffered services.

10.2.7.3. The MTF must ensure that the donor has adequate liability insurance coverage for such personnel (Federal Acquisition Regulation 84-42, subpart 37.4; *Non-Personal Health Care Services*), and ensure compliance with existing Air Force policies relating to licensure, credentials review, and clinical privileges delineation (AFI 44-119).

10.2.8. To avoid any appearance of a conflict of interest or violation of dual compensation rules, Air Force medical personnel assigned to or employed at the MTF and conducting the clinical investigation under this instruction may not engage in off-duty employment, or otherwise be compensated by non-Air Force sources, in connection with their work on such clinical investigations.

Chapter 11

PUBLICATIONS

11.1. Air Force Support. Encourages publication of papers resulting from clinical investigation projects in military and civilian professional journals.

11.2. Mandatory Volunteer Statement. All printed papers, articles, and reports pertaining to the use of volunteers within the provisions of this instruction must contain the following statement "The voluntary, fully informed consent of the subjects used in this research was obtained as required by AFI 40-403." See AFI 35-205 for proper clearance procedures.

Chapter 12

MAINTENANCE OF RECORDS

12.1. Responsible Office. The IRB maintains official case-files documenting the review, approval, conduct, and results of clinical investigations involving human test subjects. These files represent an irreplaceable source of medical knowledge and may be required for medicolegal purposes.

12.2. Contents of a Case File. Each clinical investigation record must contain, as a minimum:

- A copy of the original protocol.
- Any changes to the protocol.
- Results of local and Surgeon General's CIC reviews.
- Informed consent documents signed by the participants.
- Copies of any pertinent patient medical information.
- Progress and final reports.
- Documentation of funds utilization.

12.3. Document Disposition. Documents are disposed of according to AFI 37-138, *Records Disposition--Responsibilities and Procedures.*

Chapter 13

INSTITUTIONAL REVIEW BOARD

13.1. Function of the Institutional Review Board. The IRB is a formal committee established at the medical facility to review proposed studies. It functions as an institutional review board as outlined in the *Protection of Human Subjects*, Code of Federal Regulation (CFR), Title 32, Part 219.

13.1.1. The board evaluates the scientific merit and necessity of all proposed investigations, and the acceptability of studies involving human experimentation according to this instruction.

13.2. Composition of the Institutional Review Board. The IRB should have at least five members. Each member must have the medical and scientific background required to ensure proper evaluation of a variety of studies. The board should also include legal and chaplain representatives.

13.2.1. IRB chairperson must be a physician, preferably the Chief of Hospital Services.

13.2.2. The IRB should not consist entirely of men or entirely of women, although this requirement may be waived by the MTF/CC when compliance is impractical.

13.2.3. A majority of the committee members must be present to conduct a meeting.

NOTE:

Exception is allowed for expedited review of protocols involving no more than minimal risk (CFR, Title 45, Part 46).

13.2.4. No investigator serving as an IRB member may participate in the initial or continuing review of any research proposal in which the member has a conflicting interest, except to provide information requested by the IRB.

ALEXANDER M. SLOAN, Lt General, USAF, MC
Surgeon General

Attachment 1

GLOSSARY OF REFERENCES, ABBREVIATIONS, ACRONYMS, AND TERMS

References

10 U.S.C. 2601, Federal Agency Record 84-42, *Federal Acquisition Regulation, Non-Personal Health Care Services*

CFR, Title 32, Part 219, *Protection of Human Subjects*

CFR, Title 45, Part 46, *Federal Policy for the Protection of Human Subjects: Additional Protections for Children Involved As Subjects in Research*

21 CFR, Parts 300-499, *Drugs for Human Use*

AFPD 40-4, *Clinical Investigation and Human Use in Medical Research*

AFI 35-205, *Air Force Security and Policy Review Program*

AFI 36-2601, *Air Force Personnel Survey Program*

AFI 37-138, *Records Disposition--Responsibilities and Procedures*

AFI 40-401, *The Use of Animals in DoD Programs*

AFI 40-402, *The Use of Human Subjects in Research, Development, Test, and Evaluation (RDT&E)*

AFI 40-403, *Clinical Investigation and Human Test Subjects in the Medical Service*

AFI 44-119, *Quality Assurance and Risk Management in the Air Force*

AFI 48-112, *The US Air Force Hyperbaric Medicine Program*

AFI 51-601, *Gifts to the Air Force*

Abbreviations and Acronyms

AFI—Air Force Instruction

AFMAN—Air Force Manual

AFPD—Air Force Policy Directive

CFR—Code of Federal Regulation

SSN—Social Security Number

CIC—Clinical Investigation Committee Definition

AFMLO—Air Force Medical Logistic Office

IRB—Institutional Review Board

MTF—Medical Treatment Facility

NIH—National Institutes of Health

CIF—Clinical Investigation Facilities

RDT&E—Research, Development, Test and Evaluation

CIP—Clinical Investigation Program

AMC—Air Mobility Command

AFMC—Air Force Material Command

AETC—Air Education and Training Command

AFMOA—Air Force Medical Operations Agency

FDA—Food and Drug Administration

IND—Investigational New Drug

IDE—Investigational Device Exemption

DoD—Department of Defense

OUSDA—Office of the Under Secretary of Defense for Acquisition

MEMO—Medical Equipment Management Office

DEFAS—Defense Finance and Accounting Service

Terms

Assent—A minor's affirmative agreement to participate in a clinical investigation.

Associate Investigators—Members of the Medical Service or other governmental agencies, and individuals at civilian universities, private institutions, or pharmaceutical companies who collaborate with the principal investigator.

Clinical Investigation—A systematic investigation or study designed to develop or contribute to generalizable knowledge that is performed by, or together with, Medical Service personnel, usually in Medical Service facilities. The term does not include individual or group training of military personnel, such as combat readiness, effectiveness, proficiency, or fitness exercises.

Emergency Use of Investigational Drugs or Devices—Emergency use of investigational drugs or devices on a human subject may be deemed necessary in a life-threatening situation. Emergency use is only for cases in which no standard acceptable treatment is available, and in which there is not enough time to obtain normal protocol approval.

Informed Consent:—

- *Informed Consent Process.* The informed consent process is intended to give a subject all the information that he or she reasonably would want about a study; to ensure that the subject understands this information; and to give the subject an opportunity to agree or decline to participate in the study. The process provides for interaction between the investigator and the subject.
- *Informed Consent Document.* A written consent document approved by the IRB. This document enables the investigator to obtain the legally effective consent of the subject or the subject's legally authorized representative. The informed consent document provides the prospective subject or the subjects representative with sufficient information to decide whether to participate in the proposed study. Consent may take two forms as outlined below:
    - *Subject Consent.* Informed consent given by a prospective human subject who has the legal capacity to give such consent. For active duty military personnel participating in a US Air

Force clinical investigation or collaborative study, there is no minimum age limitation. Consent must be given voluntarily, freely, and without any use of force, fraud, deceit, duress, constraint, coercion, or unlawful or improper inducement. The subject must possess sufficient understanding of the implications of his or her participation in the study in order to make an informed decision. A subject is free to withdraw participation at any time without jeopardizing his or her rights to treatment.

- *Third Party Consent.* Consent given by the parents, legal guardian, or other legally authorized third party who represents the prospective human subject's welfare and interest. Third party consent may be used if the prospective human subject legally is not capable of giving consent. This third party consent is subject to all of the same criteria for full and complete disclosure as is the subject's own consent, and must be freely given.

Institutionalized Mentally Infirm Person—Any person who is confined, whether by court order, voluntary commitment, or otherwise, in an institution for the care of the mentally ill, the retarded, the emotionally disturbed, the psychotic, or the senile, and others with impairments of similar nature, regardless of whether or not such person has been determined to be legally incompetent and regardless of whether or not he or she is capable of giving legally effective consent.

Investigational Drugs or Devices—Drugs or devices which are not FD-Aapproved for marketing. These include drugs or devices for which the FDA has provided either a notice of exemption as an Investigational New Drug (IND), or an Investigational Device Exemption (IDE), as appropriate.

Life Threatening—A situation where delay of immediate treatment would result in loss of life or serious bodily injury to the patient.

Medical Misadventure—An unauthorized deviation from an approved clinical investigation protocol that has the potential to cause or has brought about injury or loss of life to a study subject.

Mentally Disabled Person—Any person who, due to mental illness, mental retardation, emotional disturbance, psychosis, senility, or other impairment of a similar nature, is not capable of giving legally effective informed consent.

Minor—Any person, other than active duty military personnel, who has not attained the legal age of consent to treatments or procedures involved in the investigation. This age is determined under the applicable law of the jurisdiction in which the investigation is to be conducted.

Principal Investigator—An individual who initiates a proposal for and conducts a clinical investigation after approval by the MTF Commander, the Surgeon General's CIC, and the Air Force Surgeon General, as appropriate. If an investigation has only one principal investigator, that person must be a member of the Medical Service. If an investigation has associate investigators, at least one investigator must be a member of the Medical Service.

Prisoner—Any person who is involuntarily confined in a penal or correctional institution, whether the institution is for the confinement or rehabilitation of juvenile offenders, for persons charged with or convicted of civil or criminal offenses, or for other purposes.

Technical Assistants—Civilian employees or agents of nonfederal organizations, such as national cancer study groups, who provide to the Air Force, at no cost to the government, a wide variety of administrative, technical, or professional services in support of a clinical investigation protocol or program. The personnel rendering the services are not normally subject to the control and supervision of federal supervisors, which usually occurs in relationships between the government and its employees.

Unanticipated Medical Event—An unforeseeable, unpreventable event that causes injury or loss of life to a study subject, after all the guidelines set forth in an approved clinical investigation protocol have been followed. An adverse drug reaction is an example of such an event.

Attachment 2

SAMPLE FORMAT--PROTOCOL SUMMARY

Title:

Principal Investigator: DSN:

Facility: If this is a collaborative/or multicenter study, identify the other participating facilities.

1. **Summary.** In 250 words or less, describe the purpose of the study, subject population (include total number and age group), procedures to be used, and duration of the study. Describe risks, discomforts, and safeguards as well as alternative available treatments.
2. **Additional Information.** If you will be using investigational drugs or devices, the following additional information is required:
   a. The drug or device to be used, including the trade and generic name and the manufacturer.
   b. If the drug or device is FD-Aapproved, but it will be used outside of its approved labeling, indicate that this is an "investigational use" and give rationale (for example, route of administration, higher dose level, or treatment of another condition not approved by FDA).
   c. FDA compliance. If an investigational new drug (IND) number or an investigational device exemption (IDE) number has been assigned, indicate the number and identify the holder; that is, Principal/or Associate Investigator, Medical Center, or manufacturer.
   d. Side effects of the proposed drug or device, from most common to rarest.
   e. Dosage rate schedule.
   f. Modifications in treatment, if side effects occur.
   g. Patient selection, including inclusion and exclusion criteria.
   h. Schedule of patient evaluation studies to be performed before, during, and after completing the study.

Attachment 3

SAMPLE FORMAT-PROPOSAL FOR CLINICAL INVESTIGATION

(Title of Investigation)

1. Purpose of Investigation. Give a brief summary.

2. Technical Approach. Summarize all information needed for an adequate evaluation. Include details of the experimental design, a description of methods to be used, and the number, age, and sex of subjects and controls. For protocols involving human test subjects, describe risks, discomforts, and safeguards, as well as alternative available treatments. Provide information on collaborative efforts with others engaged in similar research, such as medical and dental schools, drug companies, and national study groups. Collaborative protocols should clearly delineate the responsibilities between the various institutions or groups, as well as medical treatment facilities.

3. Investigation Schedule:

a. Date investigation will begin.

b. Duration.

c. Time phases.

d. Date of completion.

Note: List any factors which may adversely influence this schedule.

4. Experimental Subjects. If experimental subjects are involved, include a statement indicating compliance with the applicable regulation. Provide a copy of the signed legal review of the protocol and consent document.

a. Human Test Subjects. If human subjects are involved, specify the age range of the participants in the protocol. Include the age of minority under local law, if applicable. Include patient inclusion and exclusion criteria and schedule of patient evaluation studies to be performed before, during, and after completing the study.

b. Animals. If animals are involved, the protocol must include:

- The purpose or objective being addressed.
- The pertinent background of scientific literature or experience that led to the experiment.
- The reason for selecting the animal species involved.
- The procedures to be used including use of anesthetics, analgesics, or tranquilizers to minimize pain and discomfort. Otherwise, give the rationale for not using these classes of drugs in experiments that are likely to cause pain or associated discomfort. Include the USDA pain classification.

5. Use of Investigational Drugs. If the investigation concerns human studies of treatment or diagnostic procedures involving the use of medications or radiopharmaceuticals not approved by the FDA, include the approved IND number and the following information about the investigational drug:

a. Chemical composition of the drug.

b. Other names of drug.

c. Side effects, from most common to rarest.

d. Dosage rate schedule.

e. Modifications in treatment, if side effects occur.

f. Medications to be used or not used during the study.

6. Use of Investigational Devices. If investigational devices are used on human subjects, provide the Investigational Device Exemption (IDE) number, a copy of the FDA letter assigning the IDE number or a copy of the manufacturer's letter approving the principal investigator or medical facility to perform the study under the auspices of their IDE number.

7. Equipment and Supplies. List items of required equipment and supplies and the estimated cost of each item. If requesting funds from the Air Force Surgeon General's Clinical Investigation Committee, include an itemized list and Element of Expense/Investment Account codes.

8. Personnel Data:

a. Medical Facility Commander (name, grade, and title).

b. Investigator and Associate Investigators (name, grade, and title).

9. Manpower. Estimate number of work hours to be applied to the investigation, categorized by Air Force specialty code (AFSC); for example:

1 Captain, AFSC _____ Hours _____

1 Staff Sergeant, AFSC _____ Hours _____

1 GS-5 Secretary _____ Hours _____

10. Bibliography. After a careful search of the scientific literature for related studies, list the major publications in the field of the investigation.

11. Include With the Protocol:

a. Informed consent document sample and a copy of legal review.

b. Curriculum vitae of principal investigators

c. Other attachments, if applicable:

(1) IND/IDE supportive documents.

(2) AF Form 601 for investment equipment.

Attachment 4

SAMPLE FORMAT-INFORMED CONSENT DOCUMENT

(Title of Proposal)

1. This paragraph should set forth the:

a. Nature.

b. Purpose(s).

c. Approximate number of subjects involved.

d. Duration of the study. Duration should include the length of participation and approximate number of visits involved.

2. Explain all procedures that you will use involving the patient and the purpose of these procedures. If certain procedures are experimental, you should so state.

3. Describe any discomfort and risks which may reasonably be expected. If drugs are involved, the following information may be included in this paragraph or as an attachment:

a. Drug name.

b. Other names of drug.

c. How administered (intravenously, intramuscularly, or orally).

d. How often administered.

e. Side effects.

(1) Those the subject may observe.

(2) Those the investigator will watch for.

NOTE: If drug is experimental or is not ordinarily used for this purpose, so state. Set forth any other information you deem important with respect to this drug.

4. Describe any benefits to the individual or to others that can reasonably be expected.

5. Describe appropriate alternative procedures, if any, that may be beneficial to the subject. Include the statements listed here as paragraphs 6 to 9:

6. "Records of my participation in this study may only be disclosed in accordance with federal law, including the Federal Privacy Act, 5 U.S.C. 552a, and its implementing regulations. DD Form 2005, **Privacy Act Statement--Health Care Records**, contains the Privacy Act Statement for the records. I understand that records of the study may be inspected by the US Food and Drug Administration (FDA)."

7. Include this statement: "I understand that my entitlements to medical and dental care and/or compensation in the event of injury are governed by federal laws and regulations, and if I desire further information, I may contact _____."

8. "In the event that an unanticipated event (clinical or medical misadventure) occurs during my participation in this study, I will be informed. If I am not competent at the time to understand the nature of the event, such information will be brought to the attention of my guardian or next of kin."

9. "The decision to participate in this study is completely voluntary on my part. No one has coerced or intimidated me into participating in this program. I am participating because I want to. Dr. _____has adequately answered any and all questions I have about this study, my participation, and the procedures involved. I understand that Dr._____ will be available to answer any questions concerning procedures throughout this study. I understand that if significant new findings develop during the course of this study which may relate to my decision to continue participation, I will be informed. I further understand that I may withdraw this consent at any time and discontinue further participation in this study without prejudice to my entitlements to care. I also understand that the investigator of this study may terminate my participation in this study if he or she feels this to be in my best interest."

_____ _____

Subject's Signature and SSN Date

_____

Sponsor's SSN (when appropriate)

NOTE:

Paragraphs 6 through 8 should be standard in all consent forms. If minor subjects may be involved, add:

"If patient is a minor and in the opinion of the attending physician the minor can understand the nature and consequences of his or her participation in the study, the minor should be fully informed and indicate his or her assent by signing this line. If such minor patient is physically unable to sign, the parent or guardian may sign for him or her as evidence of the minor's assent."

_____ _____

Parents' or Guardian's Signature and SSN Date

Generally both parents or guardian will sign if minor subjects are involved.

_____ _____

Advising Investigator and SSN Date

_____ _____

Witness Date

(Must witness both the volunteer's and physician's signature)

Distribution:

1. IRB
2. Subject's Medical Record (to be maintained permanently)

3. Principal Investigator
4. Subject

Attachment 5

SAMPLE FORMAT-EMERGENCY USE REQUEST

Patient's Name and SSN: (If Dependent, use Sponsor's SSN.)

Responsible Physicians: (Include department, phone number, and name of Medical Treatment Facility.)

Initial Justification for Use:

Diagnosis:

Risks: (Include known or anticipated side-effects of proposed therapy, and patient risk if this emergency therapy is not received.)

Alternative Therapy:

Explain Why Standard Therapeutic Plan Not Used:

Safeguards: (Include follow-up measures that will be used to minimize risks of therapy.)

Duration of Planned Therapy:

Dose and Frequency Regimen: (Include dose and frequency modification plan if side-effects occur.)

Nature of Drugs or Devices: (Include trade and generic names, name of manufacturer and supplier, IND (investigational new drug) or IDE (investigational device exemption) number, and name of individual, manufacturer, or supplier who holds the IND or IDE number.)

Other: If this proposed therapy required consultation with the Centers for Disease Control (CDC), National Cancer Institute (NCI), or Food and Drug Administration (FDA), include the name, department, and phone number of the individual contacted.)

Approved or Disapproved:

_____

Signature

Name, Rank

Medical Facility Commander

Attach copies of the following:

1. Signed informed consent document.
2. Drug or device information from manufacturer or supplier.

Attachment 6

SAMPLE FORMAT--PROGRESS/FINAL REPORT

TO: HQ AFMOA/SGPT

Subject: Clinical Investigation Proposal (Surgeon General's CIC Assigned Number and Title)

1. Status of study, including summary of findings to date and problems experienced or anticipated.
2. Number of subjects participating in the study.
3. Status of subjects entered into the protocol.
4. Status of resources allotted for the study. Include comments on funds and equipment received from the Surgeon General's Clinical Investigation Committee, if any.
5. Estimated completion date of the study and percent completed.
6. Publications and presentations made (attach a copy).
7. For final reports, include the following:
   a. A statement as to whether the objective of the study was met.
   b. A summary of the entire study to include how the findings may benefit the Air Force.
   c. If the study was terminated prior to completion explain why.

Attachment 7

SAMPLE FORMAT--MEMORANDUM OF UNDERSTANDING FOR GIFTS OF TECHNICAL ASSISTANCE

MEMORANDUM OF UNDERSTANDING

BETWEEN

(AIR FORCE MEDICAL TREATMENT FACILITY)

AND

(DONOR)

1. **Purpose:** This Memorandum of Understanding (MOU) is established to coordinate the services of technical assistance provided to the Air Force in support of the Air Force Clinical Investigation Program (CIP). Technical assistants are defined as employees or agents of nonfederal organizations who provide a wide variety of services to the Air Force in support of a clinical investigation protocol or program. These services include administrative, technical, or professional support, and are provided at no cost to the government.
2. **Reference:** AFPD 40-4.
3. **Background:**
   a. Air Force Information:
      (1) It is Air Force policy to encourage and support clinical investigations that contribute to the progress of the biomedical sciences and to the efficiency of the Air Force or other military Medical Services.
      (2) The Air Force Surgeon General, or designee, through a Clinical Investigation Committee, will review and render an approval or disapproval decision on clinical investigation proposals.
      (3) Clinical investigation is an essential component of optimal health care, and consists of organized scientific inquiry into clinical problems involving the health care of Department of Defense beneficiaries. The goals of the Air Force CIP include:
         (a) Achieving continuous improvement in the quality of patient care.
         (b) Providing experience in the essential discipline of organized scientific inquiry to personnel who will ultimately become teaching chiefs and consultants in Air Force MTFs.
         (c) Strengthening the Graduate Medical Education (GME) program.
   b. Donor Information:
      (1) Description of organization making offer of service(s). (Example: The ABC Organization is a not-for-profit corporation created to encourage and support clinical research and medical education.)
      (2) The (donor) is or is not a defense contractor. (Choose one either is or is not.)
      (3) The (donor) has the capability to provide the services of trained personnel (professional, technical, and administrative) to support Air Force Surgeon General-approved clinical research at (AF MTF) at no cost to the government.

4. **Procedures:** Management of clinical investigations technical assistance services:
   a. (Donor) may proffer technical assistants in support of the clinical investigation program at AF MTF.)
   b. Such technical assistants must abide by all applicable and Air Force rules and regulations.
   c. (Donor) must ensure that such technical assistants clearly understand that the services rendered will be performed without any form of compensation from the US Government.
   d. (Donor) will provide workman's compensation, pay social security taxes, and provide liability insurance and credentials, when required, on all personnel provided as technical assistants to (AF MTF). The donor agrees to inform the Air Force of any change in its technical assistance insurance coverage during the period of service.
   e. The (donor) agrees to indemnify and hold harmless the United States, its agents and employees against all liability resulting from the services of its technical assistants. ***Note: You should obtain this provision as part of the agreement when possible; however, if you cannot, then decide whether it is in the best interest of the Air Force to enter into the agreement without the hold-harmless clause.*** You should contact your staff judge advocate or medical law consultant before making this decision.
   f. To avoid the appearance of a conflict of interest or violation of dual compensation rules, Air Force medical personnel assigned to or employed at (AF MTF) may not engage in off-duty employment or otherwise be compensated by (Donor) in connection with their work on any clinical investigation.
   g. (Donor) will notify the (AF MTF), in writing, of any proposed offer of technical assistance. Prepare such a letter of proffer for each individual who will provide technical assistance. The letter should include the following: name of individual, the nature of their support, and the expected duration of their participation in the one or more clinical investigation protocols or programs for which support is being proffered.
   h. (Donor) proposals for technical assistance services related to clinical investigation protocols will be approved by the MTF Commander.
   i. (Donor) agrees to provide information on the number of technical assistance personnel supporting clinical investigations at (AF MTF) upon request, as a means of confirming internal Air Force audit information.
5. **Standards of Conduct:** Nothing in this agreement pertaining to clinical investigation, technical assistance, or medical education support obviates Air Force requirements pertaining to prevention of conflict of interest or adherence to standards of conduct.
6. **Agreement:** The Commander (AF MTF), and the (Title of Individual) of (Donor) hereby agree to enter into this MOU to establish procedures for (Donor) to provide technical assistance in support of patient care and clinical investigation at the (AF MTF).
7. **Effective Date:** This agreement becomes effective upon the signature of both parties and remains in effect until canceled.
8. **Modification of This Agreement:** This agreement will be reviewed biennially at least 90 days prior to the anniversary date. It may be revised at any time upon the written mutual consent of the parties concerned.

9. **Termination of Agreement:** This agreement may be terminated at any time by either party concerned, upon giving at least (suggest 90 days) written notice to the other party. Such notice shall be sent by registered mail.
10. **Approval:**

_____ _____

MTF Commander Date

_____ _____

Donor (name and title) Date